The cardiovascular health of retired field-based athletes: a systematic review and meta-analysis.

Abstract

Background: Retirement from elite sport participation is associated with decreased physical activity, depression, obesity and ischemic heart disease. Although engagement in physical activity through sport is recognised as cardio-protective, an estimated one quarter of American football players deaths are associated with cardiovascular disease (CVD), predominately players classified as obese.

Hypothesis/Purpose: To systematically investigate the cardiovascular health profile of retired field-based athletes.

Methods: This review was conducted and reported in accordance with the preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) and pre-registered with PROSPERO.Four databases (Pubmed, CINAHL, EMBASE, WOS) were systematically searched from inception to October 2018 using MeSH terms and keywords. Inclusion criteria included; retired field-based athletes, over the age of 18 years, and at least one CVD risk factor according to the European Society of Cardiology and American Heart Association. Review articles were not included. Control groups were not required for inclusion but when available analysis was included. Eligible articles were extracted using Covidence. Methodological quality was assessed independently by two reviewers using the AXIS tool. The accuracy of individual study estimates was analysed by random-effect meta-analyses.

Results: This review yielded thirteen studies. A total of 4,350 male retired field-based athletes from two sports; American football and soccer (mean ages: 42.2–66 years) were included. Seven studies compared retired athletes to control groups. Retired athletes had elevated systolic blood pressure (BP) in 4 of 6 studies. 50% of studies found greater high-density lipoprotein (HDL), 80% found lower triglyceride levels and all studies found greater low-density lipoprotein (LDL) for retired athletes compared to controls. The prevalence and severity of carotid artery calcium (CAC) and carotid artery plaque (CAP) was similar to controls . Retired linemen had double the prevalence of cardio-metabolic syndrome compared to non-linemen.

Conclusions: Overall findings are mixed. Inconsistencies in reporting of CVD risk factors and methodological biases reduced study quality. Retired athletes have comparable CVD risk profile to the general population**.** Retired athletes with elevated playing time body mass had an increased prevalence and severity of risk factors. Significant gaps remain in understanding long term cardiovascular effects of elite athleticism.

Key Words: cardiovascular; heart disease; retired athletes; field-based; evidence- based review; risk factors.

What is known about the subject? There is no review paper assessing the cardiovascular health profile of retired field-based athletes. One quarter of retired football player's deaths are caused by CVD, predominately those classified as obese. There has been a 10% increase in the body mass of football players over the past decade. Retired athletes often fall into obese classification following retirement, although it is not known if they experience the same risk factors for CVD as the general population or if their prior elite athleticism provides a prolonged cardio-protective benefit even in the presence of obesity.

What this study adds to existing knowledge? Retired athletes are found to have a substantial risk for future to adverse CV event, similar to general population indicating athletic past does not provide long-term protection from CVD. Risk factors associated with CVD; increased systolic BP, LDL, CAC and cardio-metabolic syndrome are present, particularly those with elevated BMI during playing career. Conflicting findings are found across studies, highlighting need for further research to clarify findings.

Introduction

Regular physical activity is recommended for the optimisation of cardiovascular health and reduction of all-cause mortality, whereas obesity is an established risk factor for cardiovascular diseases (CVD). [14, 29, 73, 80] Field-based athletes from sports such as; American football and rugby, present with greater body mass alongside superior aerobic fitness. [13, 29, 49, 68, 77, 85] However, the cardiovascular health of these athletes post retirement is unclear. Premature mortality from CVD has become a prominent topic of discussion for field-based athletes, particularly during the transition into retirement. [4] Athletes are typically perceived as a healthy cohort, with evidence supporting that fitness provides protection against known health risks of obesity [14, 41] and relevant co-morbidities. [62, 67] Research also demonstrates that although exercise has beneficial cardio-protective qualities, it does not necessarily translate into immunity of cardiovascular risk. [32] An estimated one quarter of American football players deaths are associated with CVD; predominately those classified as obese.[28] Furthermore, when compared with retired baseball players, retired football players are more than twice as likely to die before age 50.[28] The National Institute for Occupational Safety and Health (NIOSH) study found that although overall mortality from CVD in retired American football players was 46% lower than the general population, linemen had a 52% greater risk. [4] It has been suggested that this may in part, reflect increased cardiovascular risk factors associated with greater body size. [4, 30] The body mass index (BMI) of American football players often falls into the obesity range. [13, 29, 48, 77, 85] However, the applicability of BMI in this cohort is widely condemned, due to high muscle mass, leading to an overestimation of body fat percentage. [55, 56, 58, 70] However, it is unknown if BMI remains inapplicable to former athletes.

To our knowledge, there has been no published review on the evidence concerning cardiovascular health in retired field-based athletes. The long-term cardiovascular health risks for professional athletes remain largely unclear. Therefore, the primary purpose of this review was to systematically collate and appraise the evidence on the cardiovascular health and the prevalence of

CVD risk factors in retired field-based athletes. Furthermore, this review aimed to investigate the prevalence of factors which influence mortality from CVD including: obesity;[33, 36] hypertension; [46] dyslipidemia;[66] glucose intolerance[20]; cardio-metabolic syndrome (CMS);[20] carotid artery calcium (CAC)[69, 76] and sleep-disordered breathing (SDB). [64, 74]

Methods

This review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement (www.prisma-statement.org) [51] and registered with PROSPERO, a registry of systematic reviews. Registration is available at https://www.crd.york.ac.uk/prospero/; registration number: CRD42017077885. Articles were retrieved via online database search engines, including; CINAHL, EMBASE, Pubmed, and WOS. The reference list of all reviews related to cardiovascular health and articles meeting the eligibility criteria were reviewed manually for suitability.

Key words and MeSH terms were searched alone and in combination. The key words included: CVD, cardiovascular health, blood pressure, lipids, cholesterol, cardio-metabolic syndrome, hypertension, glucose intolerance, body composition, body mass index, body fat percentage, low-density lipoprotein, high-density lipoprotein, triglycerides, total cholesterol, sleep-disordered breathing, field-based athlete, American football, baseball, field hockey, rugby, Gaelic football and soccer. The inclusion criteria consisted of; retired athletes from a field-based sport, over the age of 18 years and studies that investigated at least one known risk factor for CVD according to the European Society of Cardiology [62] and the American Heart Association [81]. The search was not limited by language or publication status and no date restriction implemented. Articles were excluded if the study design was a review paper and retired athletes with a prior CV event were included. Articles did not require the inclusion of controls.

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A three-step screening strategy was implemented to identify appropriate relevant articles for screening using Covidence (www.covidence.org) (Figure 1). Title and abstracts were screened by two authors blind to each other's selection, in accordance with the aforementioned inclusion criteria. Then, reviewers independently screened full texts (Appendix 1). A third reviewer was consulted to make a final decision when consensus was not reached between the two reviewers. Manual searches were performed of reference lists of the selected articles. The search methodology and process are described in Figure 1. Eligible articles were critically appraised, and quality assessed in a full text screening using the AXIS Tool for Critical Appraisal of Cross-sectional Studies (Table 1). [17] When studies were agreed upon, one reviewer extracted data from selected studies to create an evidence table, using Strobe guideline analysis. [79]

We assessed the precision and accuracy of individual study estimates by implementing random-effect meta- analyses to examine the overall effect. Heterogeneity between studies was determined by the I^2 statistic [31] as an indicator of the proportion of total variation in estimates that is caused by heterogeneity. I^2 values of 25%, 50% and 75% correspond to low, moderate and high degrees of heterogeneity. Where high levels of heterogeneity were detected ($I^2 > 75\%$) a sensitivity analysis was implemented. Findings from the random-effects meta-analysis is represented through forest plots. Studies removed during sensitivity analysis are represented by 0.0% weight in forest plot figures.

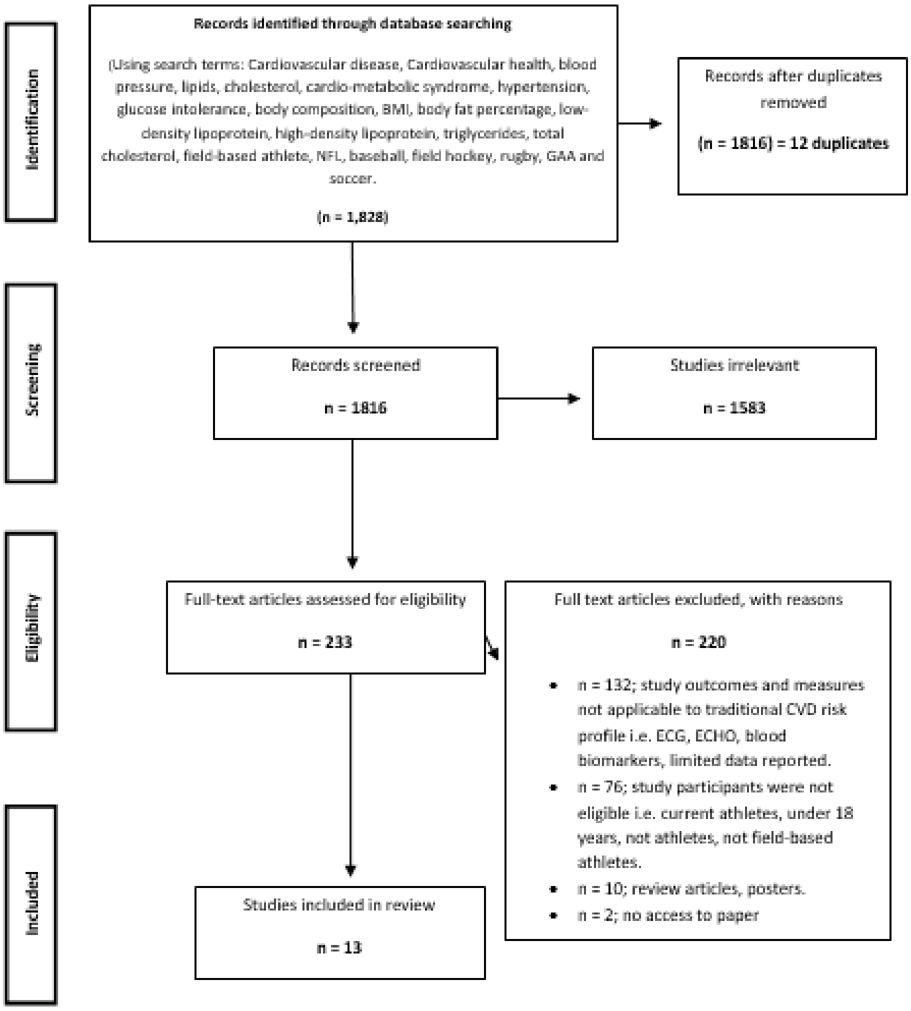

Figure 1: PRISMA Flow Diagram

Table 1: Critical Appraisal of Included Studies

	Miller[50] (2008)	Panayiotoglou[60] (2017)	Barsa[5] (2014)	Chang[10] (2009)	Hurst[34] (2010)	Hyman[35] (2012)	Albuquerque[1] (2010)	Carruthers[8] (2017)	Kelly[38] (2014)	Lynch[45] (2007)	Pokharel[63] (2014)	Virani[78] (2012)	Luyster[44] (2017)
Introduction													
Were the aims/objectives of the study clear?	N	Y	Y	Y	U	Y	N	N	Y	N	Y	Y	Y
Methods													
Was the study design appropriate for the stated aim(s)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the sample size justified?	N	N	Y	Y	N	N	Y	N	N	N	N	N	Y
Was the target reference population clearly defined?	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
Was the sample frame taken from an appropriate population base so it closely represented the target/reference population under investigation?	Y	Y	Y	Y	Y	N	Y	U	Y	Y	Y	Y	Y
Was the selection process likely to select subjects/participants that were representative of the target target/reference population under investigation?	Y	Y	Y	Y	Y	Y	U	U	Y	Y	Y	Y	Y
Were there measures undertaken to address and categorise non-responders?	N	N	N	N	N	N	U	N	Y	N	U	U	N
Were the risk factor and outcome variables measured appropriate to the aims of the study?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the risk factor and outcome variables measured correctly using instruments/measurements that had been trialled, piloted or published previously?	Y	Y	Y	Y	Y	U	Y	U	Y	Y	Y	Y	Y
Is it clear what was used to determine statistical significance and/or precision estimates? (e.g. values , CIs)	Y	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y

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For Table 1, please confirm edits to the column headings and confirm the abbreviations as added for No, Yes, and Unsure.

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Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	Y	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y
Results													
Were the basic data adequately described?	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
Does the response rate raise concern about non-response bias?	Y	Y	N	N	Y	Y	Y	U	N	Y	Y	N	N
If appropriate, was information about non-responders described?	N	N	N	U	U	N	N	U	U	N	U	U	N
Were the results internally consistent?	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	Y	Y
Were the results for the analyses described in methods, presented?	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
Discussion													
Were the authors' discussions and conclusions justified by the results?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the limitations of the study discussed?	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
Other													
Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	N	Y	N	N	N	N	N	N	N	N	N	N	N
Was ethical approval or consent of participants attained?	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	Y	Y

Abbreviations: N, no; Y, yes; U, unsure. Coloured text indicates the following: Green – positive impact on quality of study; Red – negative impact on quality of study; Orange – unknown impact on quality of study

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Results

Overall, 1,816 articles (following the removal of 12 duplicates from the original 1,828 articles) were retrieved. Screening of titles and abstracts excluded 1,583 articles based on our aforementioned inclusion criteria. This left 233 articles for full text screening. Of the 233 studies, 76 were excluded as study participants were current athletes; 132 studies were excluded due to the studies' primary outcomes not being relevant to traditional cardiovascular health assessment; 10 studies were excluded due to study design and insufficient data presented and 2 were excluded due to no access to the full text. Overall, 13 studies were identified as relevant to cardiovascular health from two field-based sports (American football and Soccer).

Of the 13 relevant studies, 11 were cross sectional, 1 observational and 1 prospective study design. All participants were male and retired professional American football (12/13) or professional soccer (1/13) players. Twelve studies were conducted in the United States and 1 in Greece (Appendix 1). Studies included consisted of large (n = 948 athletes) and small (n = 12 athletes) cohorts. Studies compared athletes to age and sex-matched controls, mainly derived from subsets of the following population cohorts; National Health and Nutrition Examination Survey (NHANES): a longitudinal data collected between 1999-2006; The Coronary Artery Risk Development in Young Adults (CARDIA): study of cardiovascular risk development in young adults (n = 5,116); Mayo Clinic Cohort: Mayo clinic database of all patients who underwent cardiovascular risk evaluation between 2006-2008); Dallas Heart Study (DHS): probability based cohort of Dallas County adults, oversampled for African-Americans (n = 6,101) and The Aerobics Centre Longitudinal Study (ACLS): longitudinal study of medical health. Participants were selected from a subset of 5,322 of the total 17,967 participants. (Appendix 1). Analysis was carried out to assess CVD risk factors according to the ESC and AHA risk factor guidelines, to compare risk factors based on sport, playing position to control groups. The studies included evaluated cardiovascular health and CVD risk in retired athletes under the following categories (Table 3); Body Composition: BMI, body fat percentage, waist circumference, neck circumference, waist to hip ratio; Blood pressure (BP); Lipids: total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, total cholesterol/HDL, triglycerides/HDL; Glucose; Cardio-Metabolic Syndrome; [27] Carotid Artery Calcium (CAC/Carotid Artery Plaque (CAP); [26] Sleep Disordered Breathing (SDB). [72]

Body Composition:

Ten studies assessed BMI, accounting for 3,095 retired athletes (8-American football, 1-Soccer) with a mean BMI of 29.3 kg/m^2 (American football: 31.3 kg/m^2; Soccer: 27.3 kg/m^2). American football players had greater mean BMI than controls. [1, 8, 10, 44] Compared to controls, retired athletes had lower body fat percentages.[45, 60] Lower waist circumference values were reported for retired athletes compared to the Dallas DHS, CARDIA and a control group. [10, 44, 45] However, compared to ACLS retired footballers had a higher mean waist circumference (Table 2). [10] Conflicting waist-to-hip ratio findings were reported for retired American football athletes [10, 45] Waist-to-hip ratio was found to be considerably lower for retired soccer players than values for American football players. Using BMI ≥ 30kg/m^2, 67.4% of retired players were classified as obese compared to 10% when using BF% ≥ 25% via dual-energy X-ray absorptiometry (DXA). [35]

Sub-group analysis found that retired linemen had elevated measures of body composition compared to retired non-linemen; higher BMI [5, 34, 44, 50] and higher body fat percentages. [50] Conflicting findings were reported on waist circumference between retired linemen and retired non-linemen. [5, 44]

Table 2: Body Composition Measures

Lead Author	BMI (kg/m²)	WC/NC (cm)	BF (%)	WHR
Miller[50]	LM v NLM: 34.9 (4.9) v 30.7 (4.0), ***		LM v NLM: 31.4% v 27.4%, *** BF% >28%: LM v NLM: 111 (67.7%) v 145 (41.9%), ***	
Panayiotoglou[60]	Soccer v Controls: 27.3 ± 2.8 v 27.4 ± 2.7, ns p = 0.919		Soccer v Controls: 24.5 ± 4.5 v 27 ± 3.9, ns	Soccer v Controls: 0.96 ± 0.05 v 0.97 ± 0.01, ns
Barsa[5]	LM v NLM: 33.6 (30.5-37.9) v 30.3 (27.7-33), p < 0.001	LM v NLM: 109.2 (99.1-119.4) v 99.1 (91.4-106.6), p < 0.001		
Chang[10]	NFL v DHS: 31.5 ± 4.2 v 31.4 ± 4.0, ns NFL v ACLS: 31.7 ± 4.7 v 28.6 ± 3.1, ***	NFL v DHS: 103.8 ± 11.5 v 107.4 ± 10.9, ns NFL v ACLS: 105.7 ± 12.7 v 98.4 ± 8.9, ***		NFL v DHS: 1.08 ± 0.85 v 0.98 ± 0.05, *** NFL v ACLS: 1.06 ± 0.73 v 0.93 ± 0.05, ***
Hurst[34]	NFL v Mayo: 31.5 ± 4.5 v 31.0 ± 2.7, ns LM v NLM: 34.2 ± 4.5 v 30.5 ± 4.0, ***			
Hyman[35]	BMI >30 = 89 (67%) BMI correlated with LM ***	BF% > 25% =13 (10%)		
Albuquerque[1]	NFL v Controls: 32.3 ± 0.3 v 30.0 ± 0.1. p < 0.001			
Carruthers[8]	NFL v DHS: 32.5 (5.4) v 29.3 (5.4), ***			
Kelly[38]	BMI: 33.8 ± 6 BMI >30: 45 (66.2%)			
Lynch[45]	NFL v Controls: 29.4 ± 2.8 v 30 ± 3, ns	NFL v Controls: 101.2 ± 6.8 v 106.1 ± 8.0, ns	NFL v Controls: 23 ± 4 v 32 ± 7, ***	NFL v Controls: 0.95 ± 0.05 v 0.98 ± 0.06, ns
Pokharel[63]	BMI: 31 (29-35)	WC: 40 (37-44) NC: 17 (16-18)		

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Virani[78]		WC: 39.4 ± 10.6
Luyster[44]	NFL v CARDIA: 30.3 ± 3.8 v 29.9 ± 4, ns LM v NLM: 29.8 ± 2.9 v 30.5 ± 4.1, ns BMI ≥ 30: NFL v CARDIA: 60 (49.2%) v 51 (41.8%), ns LM v NLM: 13 (38.2%) v 47 (53.4%), ns	NFL v CARDIA: 95.2 ± 22 v 98.1 ± 10.2, ns LM v NLM: 92.6 ± 19.7 v 96.2 ± 22.8, ns

Abbreviations: LM: linemen; NLM: non-linemen; BMI: body mass index; WC: waist circumference; NC: neck circumference; BF%: body fat percentage; WHR: waist-to-hip ratio; NHANES: National Health and Nutrition Examination Survey; CARDIA: The Coronary Artery Risk Development in Young Adults Mayo; Mayo Clinic Cohort; DHS: Dallas Heart Study; ACLS: The Aerobics Centre Longitudinal Study; NFL: National Football League.

Data are reported as: mean ± SD, median (IQR) or n (%). ns – non-significant; * - p<0.05; ** - p<0.01; *** - p<0.001.

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Hypertension and Blood Pressure:

A greater incidence of hypertension was reported in athletes compared to controls. [1, 5, 34, 44] Retired linemen had higher prevalence of hypertension compared to retired non-linemen, although not significantly (Table 3). [5, 50 34, 44] Most studies found higher resting systolic BP in retired football players compared to controls (Table 3). [1, 8, 10, 34, 44, 45] Conflicting findings were reported for sub-group analysis in American football players. (Table 3) [5, 34, 44, 50]

Lipid Profiles:

Eleven studies analysed measures of lipid profiles. A greater prevalence of hyperlipidemia was reported for retired athletes compared to controls and population norms. [10, 34] Average total cholesterol for retired athletes was 194.3 mg.dl. Mixed findings were reported for mean *total cholesterol* for retired athletes; three studies report lower values [1, 10, 34] and three report higher values (Table 3). [10, 44, 45] Most studies examining retired football athletes found higher HDL values compared to controls. [1, 8, 10, 34, 44, 45] Mean LDL for retired American football and soccer players was 123.9 mg.dl and 134mg.dl, respectively, both above recommended levels. [1, 5, 10, 25, 34, 44, 45, 63, 78] All studies reported higher LDL values for retired athletes compared to controls. [1, 10, 34, 44, 45] Five of six studies reported lower triglyceride values in retired athletes. [1, 10, 34, 45, 60] One of three studies investigating total cholesterol/HDL ratio reported lower ratios in retired athletes compared to controls. [34, 45, 60]

Sub-group analysis based on prior playing position for American football showed that retired linemen had higher total cholesterol values in three studies[5, 34, 50] and equal in one. [44] Four studies found higher HDL values in retired compared to non-linemen. [5, 34, 44, 50] Conflicting findings for LDL were reported; two reported higher values for non-linemen[5, 34] and one showed higher for linemen

(Table 3). [44] Inconsistencies were found triglyceride levels; Two studies reported higher levels for linemen [34, 50] and two reported higher levels for non-linemen. [5, 44]

Glucose:

The prevalence of diabetes was reported to be between 7% and 8%. [1, 5, 10, 35, 50, 63, 78] Conflicting reports on fasting glucose was reported for retired football players; three studies found lower glucose values for retired football players and two found higher levels compared to comparators. [1, 10, 34, 44, 45] Higher glucose values were reported for former linemen compared to non-linemen. [5, 34, 44, 50]

Biomarkers:

Four studies measured high sensitive C-reactive protein (hsCRP.) [5, 10, 63, 78] Chang reported conflicting findings; lower values in retired athletes compared to DHS but higher values compared to ACLS. [10] Two studies found no association between hsCRP levels and CAP or subclinical atherosclerosis. [5, 78] HsCRP was found to be significantly higher in retired NFL players with pre-existing cardio-metabolic syndrome. [78]

Table 3: Risk Factors for CVD

Lead Author	Blood Pressure	Lipids	Carotid Artery Calcium	Cardio-Metabolic Syndrome
Miller[50]	**LM v NLM** HT: 41 (25%) v 71 (20.5%), ns SBP; 137.1 (21.3) v 131.9 (17.4), ** DBP: 79.2 (13.3) v 78.5 (11.4), ns	**LM v NLM:** HDL: 44.5 (14.2) v 47.6 (14.9), * TC: 189.1 (43.9) v 195.6 (38.6), ns TG: 128.5 (79.8) v 116.1 (70.8), ns		**LM v NLM:** CMS: 98 (59.8%) v 104 (30.1%), *** BMI ≥ 30 kg/m^2:140 (85.4%) v 174 (50.3%), *** Raised BP: 111 (67.7%) v 212 (61.3%), ns Reduced HDL: 69 (42.1%) v 113 (32.7%), ns Raised FG: 99 (60.4%) v 130 (37.6%), *** Raised TG: 51 (31.1%) v 83 (24%), ns
Panayiotoglou[60]		**Soccer v Controls:** TG: 1.1 ± 0.2 v 1.6 ± 0.8, ns		
Barsa[5]	**LM v NLM:** HT: 38.8% v 28.5%, ** SBP; 131 (122-144) v 130 (120-143), ns	**LM v NLM**: HDL: 45 (39-55.8) v 48 (40-57), ** LDL: 117.5 (98-143) v 127 (104-151.8), *** TC: 190 (167.5-214) v 198 (173-227), * TG: 88 (62-141) v 91 (66-140.5), ns	**LM v NLM:** CAC = 0: 105 (33.88%) v 259 (41.7%),* CAC = 1-100: 103 (33.22%) v 198 (31.88%), ns CAC ≥ 100: 102 (32.9%) v 164 (26.41%), *	**LM v NLM:** CMS: 25.8% v 16.5%, ***
Chang[10]	**NFL v DHS:** SBP: 127.6 ± 16.7 v 135.6 ± 17.0, *** DBP: 77.3 ± 11.2 v 82.5 ± 10.4, p *** **NFL v ACLS:** SBP: 129.2 ± 17.0 v 129 ± 16, ns DBP; 77.5 ± 11.1 v 85.0 ± 9.8, ***	**NFL v DHS**: HDL: 50.8 ± 16.8 v 43.7 ± 10.9, *** LDL: 128.5 ± 36.0 v 107.7 ± 37.5, p*** TC: 197.8 ± 42.1 v 176.8 ± 40.1, *** TG: 81 (61-115) v 111 (74-160), *** **NFL v ACSL:** HDL: 49.4 ± 17.0 v 46.4 ± 11.5, ns	**NFL v DHS:** 46% v 48.3%, ns No statistically significant difference across CAC scores for all groups	**NFL v DHS:** Significantly lower percentage of retired players with CMS compared to controls * **NFL v ACLS:** 39.5 % v 23%, ***

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		LDL: 126 ± 36.2 v 124.7 ± 37.2, ns TC: 192.9 ± 41.9 v 204.0 ± 41.6, *** TG: 83.5 (61-122) v 127.5 (92-177), ***		
Hurst[34]	**NFL v Mayo:** HT: 38(19%) v 6(7%). SBP: 128.7 ±16.4 v 123.7 ± 13.8,** DBP: 78.7 ± 10.9 v 78.4 ± 8.2, ns **LM v NLM:** HT: 12(20%) v 9(6%), * SBP: 128.8 ± 16.9 v 128.6 ± 16.2, ns DBP: 79.2 ± 13.1 v 78.6 ± 9.9, ns	**NFL v Mayo:** HDL: 40.9 ± 16.5 v 50.1 ± 13.5, ns LDL: 131.3 ± 25.6 v 126.4 ± 35.5, ns TC: 198.8 ± 40.8 v 207.2 ± 40.1, ns TG: 102.6 ± 64.6 v 162.2 ± 128.3, *** **LM v NLM:** HDL: 45.4 ± 18.4 v 50.5 ± 15.6, p = 0.045 LDL: 127.5 ± 30.1 v 132.8 ± 37.7, ns TC: 197.7 ± 37 v 199.2 ± 42.5, ns TG: 120.5 ± 64.4 v 95.1 ± 63.4, **	**NFL v Mayo:** Plaque: 67 (33%) v 36 (29%), ns **LM v NLM:** Plaque: 16(27%) v 51(36%), ns	**LM v NLM:** 27(46%) v 32 (23%), ***
Hyman[35]	HT: 55 (42.6%)			
Albuquerque[1]	**NFL Vs Controls:** HT: 37.8% v 21.4%, *** SBP: 133.5 ± 1.1 v 126.5 ± 0.5, *** DBP: 80.0 ± 0.7 v 72.7 ± 0.3, ***	**NFL Vs Controls:** HDL: 44 ± 0.8 v 47 ± 0.3, *** LDL: 121.4 ± 2.3 v 117 ± 1.3, ns TC: 183.4 ± 4.1 v 195.3 ± 1.5, ns TG: 149.8 ± 12.7 v 168 ± 4.7, ***		
Carruthers[8]	**NFL v DHS:** SBP: 136.1 (17.2) v 132.7 (17), *	**NFL v DHS:** HDL: 55.9 (16.6) v 48.9 (12.9), ***	**NFL v DHS:** **Median (95% CI) CAC:** 0.5 (0, 45.2) v 1.8 (0, 73), ns **<5% risk:** CAC = 0: 23 (60%) v 120 (64%), ns CAC = 1-100: 12 (32%) v 56 (30%) CAC ≥100: 3 (8%) v 11 (6%) **5-7.5% Risk:** CAC=0: 15 (65%) v 61 (48%), * CAC=1-100: 3 (13%) v 53 (41%) CAC ≥100: 5 (22%) 14 (11%) **>7.5% Risk**: CAC = 0: 14 (32%) v 83 (27%), **	

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			CAC = 1-100: 21 (49%) v 116 (38%) CAC ≥100: 8 (19%) v 104 (34%)	
Kelly[38]				34 (50%)
Lynch[45]	**NFL v Controls:** SBP: 130 ± 19 v 133 ± 20, ns DBP: 79 ± 8 v 82 ± 13, ns	**NFL v Controls:** HDL (mM): 1.30 ± 0.23 v 0.95 ± 0.19, *** LDL (mM): 3.10 ± 0.48 v 3.04 ± 0.61, ns TC (mM): 4.93 ± 0.52 v 4.75 ± 0.76, ns TG (mM): 1.17 ± 0.69 v 1.71 ± 0.67, *		
Pokharel[63]	HT: 267 (32%) SBP: 130 (121-142) DBP: 80 (74-87)	HDL: 47 (39-56) LDL: 125 (103-148) TC: 196 (171-223) TG: 89 (64-141)		
Virani[78]	HT: 309 (34.7%)	HDL: 49 ± 14 LDL: 127 ± 38 TC: 199 ± 41 TG: 89 ± 77	CAP detected in 41% of players	187 (19.7%)
Luyster[44]	**NFL Vs CARDIA:** HT: 36 (29.5%) v 35 (28.7%), ns SBP: 125.3 ± 13.9 v 120.4 ± 13.2 ** DBP: 80.1 ± 10.3 v 75 ± 11.2, *** **LM v NLM:** HT: 9 (26.5%) v 27 (30.7%), ns SBP: 124.6 ± 16.9 v 125.6 ± 12.7, ns DBP: 81.4 ± 9.7 v 80 ± 9.7, ns	**NFL Vs CARDIA:** HDL: 49.9 ± 11.5 v 44.9 ± 12, *** LDL: 126.5 ± 39.7 v 110.5 ± 31.7, *** TC: 197.9 ± 43.5 v 183.4 ± 35.9, ** TG: 140.3 ± 96.5 v 140.2 ± 92.4, * **LM v NLM:** HDL: 47.9 ± 11.9 v 50.8 ± 11.3, ns LDL: 135 ± 48.7 v 122.9 ± 34.9, ns TC: 198.1 ± 55.8 v 197.9 ± 37.6, ns TG: 105.3 ± 75.1 v 120.5 ± 104.3, ns	**NFL v CARDIA:** CAC Presence: 37 (30.3%) v 37 (30.3%), ns CAC Distribution: ns CAC = 0: 87 (71.3%) v 87 (71.3%) CAC = 1-99.99: 29 (23.8%) v 28(23%) CAC ≥100: 6 (4.9%) v 7 (5.7%). **LM v NLM:** CAC presence: 8 (23.5%) v 29 (33%), ns	

Abbreviations: LM: linemen; NLM: non-linemen; NHANES: National Health and Nutrition Examination Survey; CARDIA: The Coronary Artery Risk Development in Young Adults Mayo; Mayo Clinic Cohort; DHS: Dallas Heart Study; ACLS: The Aerobics Centre Longitudinal Study; NFL: National Football League; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high-density lipoprotein; LDL: low-density lipoprotein; TC: total cholesterol; TG:

triglycerides; CAC: carotid artery calcium; CAP: carotid artery plaque; IFG: impaired fasting glucose; CMS: cardio-metabolic syndrome. Data are reported as: mean ± SD, median (IQR) or n (%). ns – non-significant; * - $p<0.05$; ** $p<0.01$; *** - $p<0.001$

Commented [AK18]: Query 9: List in a general footnote how the data in the table are reported: mean ± SD, median (range), n (%), etc.

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Commented [AK20]: Query 6: List in a general footnote how the data in the table are reported: mean ± SD, n (%), etc. It’s unclear how the data are presented for Carruthers BMI, Barsa WC/NC, and Pokharel WC/NC

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Cardio-metabolic Syndrome:

Six studies reported on the prevalence of cardio-metabolic syndrome in retired American football players. A substantial variance was found, ranging from 19.7% to 50%. Compared to the DHS a significantly lower incidence of cardio-metabolic syndrome was reported; however, compared to ACLS and controls a higher prevalence was reported for retired football players.[5, 10] Retired linemen had almost double the prevalence of cardio-metabolic syndrome compared to non-linemen (Table 3). [5, 34, 50] Three of the component criteria; BMI ≥ 30kg.m^2, reduced HDL cholesterol and raised fasting glucose, were significantly greater in retired linemen compared with non-linemen. [50]

Carotid Artery Calcium/Carotid Artery Plaque:

Three studies found similar prevalence and severity of CAC between retired athletes and controls.[8, 10, 44] When controlled for ethnicity, no difference in CAC between retired players and DHS (Caucasians: 67.2% v 57.4%; African Americans: 31.5% v 42.1%) was reported.[10] Conflicting findings were reported for sub-group analysis of American football players. Two studies reported a greater prevalence of CAC/CAP for non-linemen. [34, 44] However, Miller reported that retired linemen were less likely to have absence of CAC, a similar likelihood of mild CAC and a greater likelihood of moderate to severe CAC compared to non-linemen (Table 3). Furthermore, adjusting for demographic and metabolic covariates, linemen playing position remained independently associated with mild (OR 1.41; 95% CI: 1.05, 2.2) and moderate to severe (OR 1.67; 95% CI: 1.05, 2.2) subclinical atherosclerosis. [5]

Sleep-disordered Breathing:

A limited number of studies analysed SDB. Self-reported presence of obstructive sleep apnoea in retired football players was reported between 41%-53%.[1 35] One study reported retired football players had double the prevalence of high risk sleep apnoea compared to the CARDIA study. [44] Retired soccer players reported less days snoring per week than controls. [60]

Smoking:

Retired athletes were reported to have lower prevalence of smoking (past or present), in all studies [1, 8, 10, 34, 44, 50, 60] Conflicting findings were identified based on playing position in American football. Two studies reported lower prevalence of smoking history in linemen compared to non-linemen,[44, 50] whereas, one study reported a greater prevalence in linemen. [34]

Meta-analysis:

Implementation of meta-analysis using random-effects and sensitivity analysis indicated that the overall effect of prior engagement in American football had a positive effect on fasting glucose levels, finding a mean difference of -4.66 (95%CI: -7.71, -1.62, I^2=55%) when compared to controls (Figure 2). Prior engagement in American football had a negative effect on systolic BP, with a mean difference of 3.07 (95%CI: 0.78, 5.36, I^2=44%) in favour of controls (Figure 3). A wide confidence interval was identified for triglycerides of athletes. A mean difference of -19.07 (95%CI: -34.96, -3.19, I^2=59%) in favour of retired athletes was found for triglycerides (Figure 4). Retired players had a higher mean value for LDL compared to control groups with a mean difference of 5.00 (95%CI: 1.54, 8.47, I^2=42%) (Figure 5).

Risk of Bias:

Studies were critically appraised using the AXIS tool. [17] Overall, studies were of moderate quality with common issues identified in several domains. Where 'unsure' response was assigned it was most commonly associated with lack of clarity in reporting. Many studies did not provide justification for the sample size due to their cross-sectional and observational study design. Studies did not address the issue of non-responders; provide information or categorise. Samples of convenience were most commonly sought, and it was not addressed how representative these samples were to the true population.

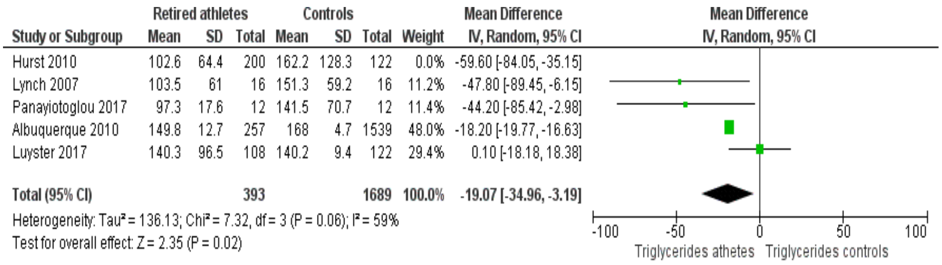

Figure 2: Forest Plot of Systolic BP.

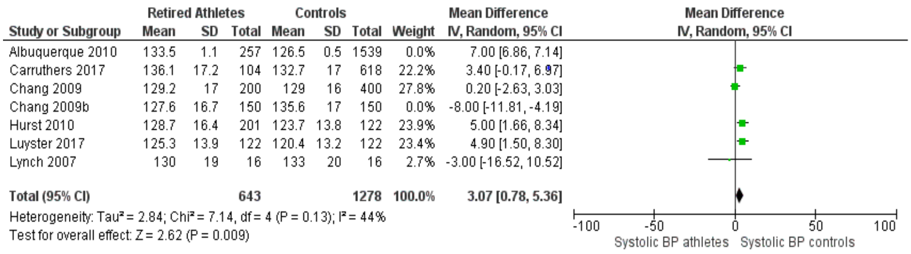

Figure 3: Forest Plot of Glucose

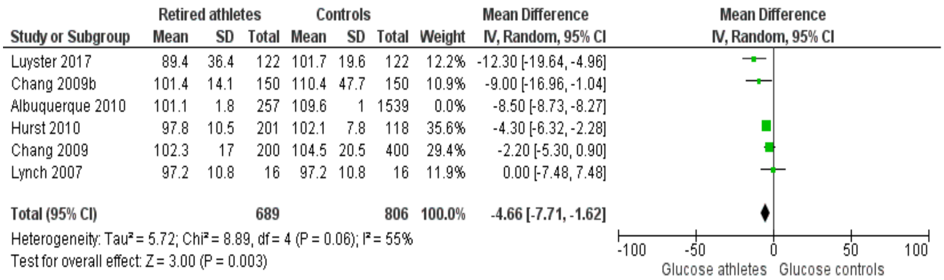

Figure 4: Forest Plot of Triglycerides.

	Retired athletes			Controls				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Chang 2009	126	36.2	200	124.7	37.2	400	19.3%	1.30 [-4.90, 7.50]
Lynch 2007	119.6	18.5	16	117.3	23.5	16	5.0%	2.30 [-12.35, 16.95]
Albuquerque 2010	121.4	2.3	257	117	1.3	1539	50.1%	4.40 [4.11, 4.69]
Hurst 2010	131.3	25.6	176	126.4	35.5	116	15.0%	4.90 [-2.59, 12.39]
Luyster 2017	126.5	39.7	107	110.5	31.7	118	10.6%	16.00 [6.55, 25.45]
Chang 2009b	128.5	36	150	107.7	37.5	150	0.0%	20.80 [12.48, 29.12]
Total (95% CI)			**756**			**2189**	**100.0%**	**5.00 [1.54, 8.47]**

Heterogeneity: Tau² = 6.22; Chi² = 6.84, df = 4 (P = 0.14); I² = 42%
Test for overall effect: Z = 2.83 (P = 0.005)

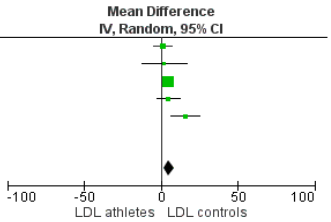

Figure 5: Forest Plot of LDL.

Discussion

Thirteen studies examined the cardiovascular health profile of retired field-based athletes. The variance in study objectives provides a broad understanding of the cardiovascular health and CVD risk profile of retired contact sport athletes and how this compares to the general population.

Synthesis of studies suggests that retired athletes with elevated BMI have a similar risk for future adverse cardiovascular event as obese non-athletes from the general population. The Framingham study in 2008 indicated that men and women who are obese have a lifetime risk of CVD of 66.8% and 46.7%, respectively. [21] Obesity measured by BMI is common among retired football players and found to be more prevalent in 5 of 6 studies (83%) compared to comparators. [1, 8, 10, 34, 44] . There is an argument that because BMI doesn't consider the increased muscle mass in current athletes, as a measure of body composition, BMI may overestimate the prevalence of obesity in current athletes. Despite a threefold greater engagement in physical activity during young adulthood (20-34 years), after the age of 65, former athletes (Age (yr): 66 ± 6) and sedentary individuals (Age (yr): 67 ± 5) have similar levels of physical activity. [45] The errors associated with using BMI during active athletic career are most likely not as significant during retirement, therefore using BMI as a measure of obesity during retirement is more appropriate Epidemiological research has consistently reported increased risk of cardiovascular death with increased BMI. [15, 40, 59, 65] Retired linemen were found to have elevated measures of body composition compared to non-lineman in all but one study. [5, 34, 44, 50] Luyster suggested that an average of 25 years following retirement, non-linemen have equal probability of becoming obese as linemen. Similarly, Miller reported that 50% of retired non-linemen had a BMI ≥ 30kg/m^2. [44, 50] The average age of retired NFL players was 57.1, falling in line with the estimated 37.7% prevalence of obesity (BMI ≥ 30kg/m^2) in males between the ages of 40-59 from the general population. [22] Despite known limitations, BMI remains the most widely used measure of obesity, with 76.9% (10/13) of studies in this review applying it. It is postulated that waist circumference and waist-to-hip ratio are more accurate indicators of obesity and future risk of

CVD for athletes than BMI. [9, 47] Interestingly, when matched for BMI both Luyster and Chang (DHS cohort) reported lower waist circumference levels. [10, 44]

This highlights the need for more reliable measures of body composition beyond BMI, waist circumference and waist-to-hip ratio, such as DXA scans. DXA scans provide in-depth analysis of body composition, identifying, lean mass, fat mass and visceral adipose tissue (VAT). In current field-based athletes, elevated BMI often reflects greater lean muscle mass. [3, 24, 37, 42, 52] Findings from this review suggests this may not be the case in retired players. This generates speculation that persistent reporting of elevated BMI found in retired athletes reflects an increase in fat mass, compared to the increased lean mass found in current athletes. No study analysed VAT in this review. Epidemiological research has consistently reported links between VAT and systemic inflammation. [19, 61, 71, 86] It remains unclear if elevated BMI during retirement diminishes benefits gained from an individual's past elite athleticism.

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The cause of long-term risk of elevated BP and hypertension in retired-field based athletes is unclear. In current American football athletes, there is an increased prevalence of hypertension (13.8%) compared to age-and-sex matched controls (5.5%). [77] The 1994 study by NIOSH reported; deaths among linemen were almost exclusively attributable to hypertension and ischemic heart disease. [4] According to the American Heart Association, risk of death from ischemic heart disease and stroke doubles with every 20 mm Hg systolic or 10 mm Hg diastolic increase among people from age 40 to 89. [81] Average systolic BP was 130.6mm Hg in this review, 10mm Hg above recommended target levels. [7, 81]

Where elevated BP was reported concomitant increases in body composition were typically reported. [1, 8, 34] When matched for BMI results on BP are conflicting. Compared to DHS cohort, retired football players had lower BP [10], however Hurst and Luyster reported higher BP. [34, 44] No study controlled for smoking, alcohol intake or dietary intake, therefore it's not possible to identify the cause of higher mean BP in retired players. Furthermore , studies comparing retired NFL players based on positions reported similar or increased BP for linemen [5, 34, 44, 50]

This suggests it's possible that body composition in linemen might offset some benefits of exercise on BP. Retired soccer players mean BMI was ≤ 30kg.m^2 (27.2kg.m^2), however according to the European Society of Hypertension Guidelines,[18] 66% had BP exceeding the upper range of grade 1 hypertension. This corresponds to statistics from age-sex matched individuals from the general population.[82] While overall non-linemen had statistically similar BMI to linemen (29.8 kg.m^2 v 30.5 kg.m^2) but a greater percentage of African-American athletes (26.4% v 47.7%, p = 0.03), the incidence of hypertension was higher for non-linemen (26.5% v 30.7%). [44] Meta-analysis identified a moderate statistical heterogeneity (I^2 =44%) (Figure 3). A possible cause for the high level of heterogeneity in these studies is the significant difference in smoking history, and BMI between retired players and controls, along with measures that were not controlled for.

An increased prevalence of hyperlipidemia and fasting glucose in retired linemen was reported in 2 studies. [10, 34] Results were conflicting for LDL and HDL concentrations. [1, 8, 10, 34, 44, 45, 60] Higher levels of HDL in retired athletes coincided with higher levels of total cholesterol [8, 10, 44, 45] This may be attributed to their physically active and high caloric diet past. Where lower levels of HDL were reported in retired players elevated measures of body composition was reported (Albuquerque; Hurst). . This suggests that size matters and early cardiovascular risk factor screening and maintenance of physical activity levels in early retirement is needed. [1, 10, 34, 50]. Multiple papers reported that hyperlipidemia is associated with coronary atherosclerosis, CAP and cardio-metabolic syndrome. [10, 45, 50, 78] All studies reported that retired players had higher LDL concentration compared to controls; this may be caused by high caloric diet during career or the change in body composition that occurs during retirement. [1, 10, 34, 44, 45] Increasing BF% coincides with a decrease in physical activity levels, similar to that of obese sedentary controls after the age of 65 years. [45]

A lower prevalence of diabetes was reported for retired athletes, despite indication of a threefold higher prevalence of impaired fasting glucose. [1, 10, 44] When stratified by ethnicity, African-American athletes had a significantly greater prevalence of impaired fasting glucose, whereas, Caucasian athletes failed to reach significance. [10] Due to the high percentage of African American athletes in retired football player groups provides a possible understanding for the difference in impaired fasting glucose levels between retired athletes and controls, warranting further investigation. All studies that reported linemen to have higher impaired fasting glucose concentration than non-linemen. [5, 34, 44, 50] Although the cardiovascular risks affiliated with cardio-metabolic syndrome and increased body size are inevitable during early retirement, engagement in physical activity during a professional sporting career may slow the progression from impaired fasting glucose to diabetes mellitus and decreases the risk of developing atherogenic lipoprotein profile. Initial meta-analysis of glucose identified a high level of heterogeneity (I^2 – 86%). Removal of Albuquerque et al reduced heterogeneity to a moderate level (I^2 – 55%), indicating a significantly lower level of fasting glucose for retired players. However, insufficient methodological information prevents investigation into possible causes.

Cardio-metabolic syndrome, an established risk factor for CVD [62] was shown to be highly prevalent amongst retired athletes. [38, 50, 60, 63] Lineman position was associated with, and in some studies double the prevalence compared to non-linemen and comparators. [5, 34, 50] Three components of cardio-metabolic syndrome; BMI ≥ 30, increased impaired fasting glucose and decreased HDL, were significantly more prevalent in linemen. [50] This is further supported by an association between cardio-metabolic syndrome and increased weight gain. [10, 60] Athletes playing in lineman position are exposed to increased likelihood of the development of cardio-metabolic syndrome after retirement. However, cardio-metabolic syndrome classification may overestimate the cardiovascular risk in larger retired players, as previously discussed; BMI is a poor indicator of body composition in this cohort. [58] The average age of retired athletes in this review was 57.1 years, therefore it is debateable how long into retirement BMI remains an inapplicable measure due to prior elite athleticism. Identification of the high prevalence in retired athletes is important, as many of the components of cardio-metabolic syndrome are reversible with lifestyle changes; physical activity and diet. Limited data suggests that obstructive sleep apnoea maybe more prevalent after retirement, possibly explained by the previously discussed elevated BMI and increased prevalence of obesity. [1, 35, 44] Retired soccer players lower mean BMI of 27kg.m^2 was associated with a lower incidence of obstructive sleep apnoea compared to controls and retired American football players. [60] However, Luyster reported that despite similar levels of obesity, high sleep apnoea risk was twice that for retired football players, compared to controls, giving plausibility to other possible causes for increased prevalence, beyond BMI. As a measure of subclinical atherosclerosis, CAP and CAC are strongly and independently associated with adverse cardiovascular events. [6, 84] Despite high levels of physical activity throughout athletic careers, following retirement, former athletes have a prevalence and distribution of subclinical atherosclerosis similar to the general population matched for age, sex and BMI. [8, 11, 34, 44, 45] The presence of CAP and CAC is a sign of advanced atherosclerosis and has significant diagnostic implications. The prevalence of CAC was consistently reported in at least one third of retired players. [10, 34, 44, 63] CAC < 100 was present in 76% of retired players, posing concern; [10] as risk of an adverse cardiovascular event increases several fold higher with CAC >100. [12] Retired linemen are more likely to have moderate to severe presence of CAC and less likely to have an absence of CAC compared to non-linemen. [5, 34]. Possible explanations for higher risk of moderate to severe CAC include; increased prevalence of obesity, hypertension, cardio-metabolic syndrome and sleep-disordered breathing. However, it is difficult to rule out factors beyond those measured in these studies, including but not limited to; steroid use, race and socio-economic status. These findings suggest former athletes have not benefited from their athletic pasts, despite the well documented cardio-protective benefits associated with pro-longed engagement in exercise. [54]

This review is limited by several factors. First, studies included were cross sectional, observational or prospective; therefore, inferences on temporality and causality cannot be made from the observed findings. Results should be viewed as hypothesis generating only. Second, 12 of the 13 studies included were based on retired football players; therefore, caution is needed when interpreting conclusions to all retired field-based athletes. It's worth noting that all studies included male athletes, retired from professional sports, therefore applicability to amateur and female athletes is limited. A high proportion of retired athletes, primarily football players, were African-American, limiting generalisability of results. Caution is needed when interpreting findings given the disproportionate percentage of African-American retired football players, who have a higher pre-disposition for increased BP and hypertension. [46] Due to the limited amount of research in this area the inclusion of a controls group was not implemented into our inclusion criteria as to widen the number of studies that could be analysed. All studies recruited participants from open health screening events allowing for self-selection bias; however, this applies to all participants; linemen, non-linemen and retired soccer players. There are possible unknown causes for findings, such as; previous use of anabolic androgenic steroids could have multiple deleterious effects on cardiovascular system; altering lipid profiles, promoting atherosclerosis, enhancing thombogenesis and altering body composition. Other possible co-founding factors include; years in retirement, diet, alcohol use, socioeconomic status, education, genetics and medication use. Use of self-reported screening tools for obstructive sleep apnoea without objective assessment, precludes confirmation that individuals who scored in the high-risk range actually had obstructive sleep apnoea. Therefore, the proportion of high-risk participants may be overestimated or underestimated. Finally, it's difficult to acquire a similar comparator population. General population and cohorts from larger studies for the most were used; however, not all studies matched controls for ethnicity, race and body composition.

Conclusion

There is inconsistency in the screening and reporting of CVD risk factors in retired field-based athletes. Most studies have focused on retired football players, with only one study examining retired soccer players. There is a need for research in field-based athletes from other sports, particularly in sports which emphasises greater player mass. There is also a need for research on cardiovascular risks in female athletes from similar sports. This current synthesis of studies has demonstrated that heavier retired field-based athletes are at a risk of elevated BP, hypertension, increased LDL, sleep-disordered breathing, cardio-metabolic syndrome and development of CAP and CAC. It can be inferred that this risk is comparable to obese non-athlete counterparts. BMI might not be an appropriate measurement of cardiovascular health in retired field-based athletes, and other measures of body composition may be more valuable. Further research is needed, focusing on retired athletes of other field-based sports such as rugby, hockey and soccer, and retired women athletes, to gain a clear insight into the cardiovascular health of all field-based sports.

References

1. Albuquerque FN, Kuniyoshi FH, Calvin AD, et al. Sleep-disordered breathing, hypertension, and obesity in retired National Football League players. *J Am Coll Cardiol.* 2010;56(17):1432-1433.

2. Anzell AR, Potteiger JA, Kraemer WJ, Otieno S. Changes in height, body weight, and body composition in American football players from 1942 to 2011. *J Strength Cond Res.* 2013;27(2):277-284.

3. Barlow et al. Percision error in dual energy X-ray absorptiometery body composition measurements in elite male rugby players. 2015.

4. Baron SR, R. . *NIOSH mortality study of NFL football players: 1959-1988.* Cincinnati, OH: National Institute of Occupational Safety and Health; 1994.

5. Basra SS, Pokharel Y, Hira RS, et al. Relation between playing position and coronary artery calcium scores in retired National Football League players. *Am J Cardiol.* 2014;114(12):1836-1840.

6. Belcaro G, Nicolaides AN, Ramaswami G, et al. Carotid and femoral ultrasound morphology screening and cardiovascular events in low risk subjects: a 10-year follow-up study (the CAFES-CAVE study1). *Atherosclerosis.* 2001;156(2):379-387.

7. Brignole M. 'Ten Commandments' of ESC Syncope Guidelines 2018: The new European Society of Cardiology (ESC) Clinical Practice Guidelines for the diagnosis and management of syncope were launched 19 March 2018 at EHRA 2018 in Barcelona. *Eur Heart J.* 2018;39(21):1870-1871.

8. Carruthers D, Joshi P, Maroules C, et al. Pooled cohort equation and coronary artery calcium in retired national football league athletes. *Journal of the American College of Cardiology.* 2017;69(11):1449.

9. Caselli S, Di Paolo FM, Pisicchio C, Pandian NG, Pelliccia A. Patterns of left ventricular diastolic function in Olympic athletes. *J Am Soc Echocardiogr.* 2015;28(2):236-244.

10. Chang AY, FitzGerald SJ, Cannaday J, et al. Cardiovascular Risk Factors and Coronary Atherosclerosis in Retired National Football League Players. *American Journal of Cardiology.* 2009;104(6):805-811.

12. Church TS, Levine BD, McGuire DK, et al. Coronary artery calcium score, risk factors, and incident coronary heart disease events. . *Atherosclerosis.* 2007;190(1):224-231.

13. Croft LB, Belanger A, Miller MA, Roberts A, Goldman ME. Comparison of National Football League Linemen Versus Nonlinemen of Left Ventricular Mass and Left Atrial Size. *American Journal of Cardiology.* 2008;102(3):343-347.

14. De Backer G, Ambrosioni E, Borch-Johnsen K, et al. European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force Of European and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of eight societies and by invited experts). *Arch Mal Coeur Vaiss.* 2004;97(10):1019-1030.

15. Denke MA, Sempos CT, Grundy SM. Excess body weight: an underrecognized contributor to high blood cholesterol levels in white American men. *Archives of internal medicine.* 1993;153(9):1093-1103.

16. DiCesare CA, Adams JR, Claytor RP, Ward RM, Cox RH. Relationship between proxies for Type II fiber type and resting blood pressure in Division I American Football Athletes. *International Journal of Health Sciences-Ijhs.* 2017;11(2).

17. Downes MJ, Brennan ML, Williams HC, Dean RS. Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). *BMJ Open.* 2016;6(12):e011458.

18. European Society of Hypertension. European Society of Cardiology guidelines for the management of arterial hypertension. Journal of hypertension. 2003;21(6):1011-1053.

19. Fontana L, Eagon JC, Trujillo ME, Scherer PE, Klein S. Visceral fat adipokine secretion is associated with systemic inflammation in obese humans. *Diabetes.* 2007;56(4):1010-1013.

20. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes care.* 2005;28(7):1769-1778.
21. Fox CS, Pencina MJ, Wilson PW, Paynter NP, Vasan RS, D'agostino RB. Lifetime risk of cardiovascular disease among individuals with and without diabetes stratified by obesity status in the Framingham heart study. *Diabetes care.* 2008.
22. Fryar CD, Gu Q, Ogden CL, Flegal KM. Anthropometric Reference Data for Children and Adults: United States, 2011-2014. *Centers for Disease Control*. 2016 ed. United States: Centers for Disease and Control; 2016.
23. Garry JP, McShane JJ. Analysis of lipoproteins and body mass index in professional football players. *Prev Cardiol.* 2001;4(3):103-108.
24. Georgeson EC, Weeks BK, McLellan C, Beck BR. Seasonal change in bone, muscle and fat in professional rugby league players and its relationship to injury: a cohort study. *BMJ Open.* 2012;2(6).
25. Gibbons GH, Shurin SB, Mensah GA, Lauer MS. Refocusing the agenda on cardiovascular guidelines: an announcement from the National Heart, Lung, and Blood Institute. *J Am Coll Cardiol.* 2013;62(15):1396-1398.
26. Greenland P, Alpert JS, Beller GA, et al. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. *Journal of the American College of Cardiology.* 2010;56(25):e50-e103.
27. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement: Executive Summary. *Crit Pathw Cardiol.* 2005;4(4):198-203.
28. Hargrove T. Supersized in the NFL: many ex-players dying young. Scripps Howard News Service Online: Scripps Howard News Service Online; 2007.
29. Haskell WL, Lee I-M, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation.* 2007;116(9):1081.
30. Helzberg JH, Waeckerle JF, Camilo J, et al. Comparison of cardiovascular and metabolic risk factors in professional baseball players versus professional football players. *American Journal of Cardiology.* 2010;106(5):664-667.
31. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in medicine.* 2002;21(11):1539-1558.
32. Hu FB, Willett WC, Li T, Stampfer MJ, Colditz GA, Manson JE. Adiposity as compared with physical activity in predicting mortality among women. *N Engl J Med.* 2004;351(26):2694-2703.
33. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation.* 1983;67(5):968-977.
34. Hurst RT, Burke RF, Wissner E, et al. Incidence of Subclinical Atherosclerosis as a Marker of Cardiovascular Risk in Retired Professional Football Players. *American Journal of Cardiology.* 2010;105(8):1107-1111.
35. Hyman MH, Dang DL, Liu Y. Differences in obesity measures and selected comorbidities in former National Football League professional athletes. *J Occup Environ Med.* 2012;54(7):816-819.
36. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of

Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Journal of the American college of cardiology.* 2014;63(25 Part B):2985-3023.

37. Jones B, Till K, Barlow M, Lees M, O'Hara JP, Hind K. Anthropometric and Three-Compartment Body Composition Differences between Super League and Championship Rugby League Players: Considerations for the 2015 Season and Beyond. *PLoS One.* 2015;10(7):e0133188.

38. Kelly DF, Chaloner C, Evans D, et al. Prevalence of pituitary hormone dysfunction, metabolic syndrome, and impaired quality of life in retired professional football players: a prospective study. *J Neurotrauma.* 2014;31(13):1161-1171.

39. Kriska AMaC, C.J. Introduction to the collection of physical activity questionnaires. *Med Sci Sports Exerc.* 1997;29(6):5-9.

40. Kujala UM, Kaprio J, Taimela S, Sarna S. Prevalence of diabetes, hypertension, and ischemic heart disease in former elite athletes. *Metabolism-Clinical and Experimental.* 1994;43(10):1255-1260.

41. Lee CD, Blair SN, Jackson AS. Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *Am J Clin Nutr.* 1999;69(3):373-380.

42. Lees MJ, Oldroyd B, Jones B, et al. Three-Compartment Body Composition Changes in Professional Rugby Union Players Over One Competitive Season: A Team and Individualized Approach. *J Clin Densitom.* 2017;20(1):50-57.

43. Levine DA, Lewis CE, Williams OD, et al. Geographic and demographic variability in 20-year hypertension incidence: the CARDIA study. *Hypertension.* 2011;57(1):39-47.

44. Luyster FS, Dunn RE, Lauderdale DS, et al. Sleep-apnea risk and subclinical atherosclerosis in early-middle-aged retired National Football League players. *Nature and Science of Sleep.* 2017;9:31-38.

45. Lynch NA, Ryan AS, Evans J, Katzel LI, Goldberg AP. Older elite football players have reduced cardiac and osteoporosis risk factors. *Medicine & Science in Sports & Exercise.* 2007;39(7):1124-1130.

47. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Journal of Hypertension.* 2013;31(7):1281-1357.

48. Mathews DK, Fox EL, Tanzi D. Physiological responses during exercise and recovery in a football uniform. *J Appl Physiol.* 1969;26(5):611-615.

50. Miller MA, Croft LB, Belanger AR, et al. Prevalence of Metabolic Syndrome in Retired National Football League Players. *American Journal of Cardiology.* 2008;101(9):1281-1284.

51. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine,.* 2009;6(7):p.e1000097.

52. Morehen JC, Routledge HE, Twist C, Morton JP, Close GL. Position specific differences in the anthropometric characteristics of elite European Super League rugby players. *Eur J Sport Sci.* 2015;15(6):523-529.

53. Muntner P, Lewis CE, Diaz KM, et al. Racial differences in abnormal ambulatory blood pressure monitoring measures: Results from the Coronary Artery Risk Development in Young Adults (CARDIA) study. *Am J Hypertens.* 2015;28(5):640-648.

54. Myers J, Prakash M, Froelicher V, Do D, Partington S, Edwin Atwood J. Exercise capacity and mortality among men referred for exercise testing. *N Eng J of Med.* 2002;346(11):793-801.

55. Nevill AM, Stewart AD, Olds T, Holder R. Relationship between adiposity and body size reveals limitations of BMI. *Am J Phys Anthropol.* 2006;129(1):151-156.

56. Nevill AM, Winter EM, Ingham S, Watts A, Metsios GS, Stewart AD. Adjusting athletes' body mass index to better reflect adiposity in epidemiological research. *J Sports Sci.* 2010;28(9):1009-1016.

57. Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, Young T. Progression and regression of sleep-disordered breathing with changes in weight: the Sleep Heart Health Study. *Arch Intern Med.* 2005;165(20):2408-2413.
58. Ode JJ, Pivarnik JM, Reeves MJ, Knous JL. Body mass index as a predictor of percent fat in college athletes and nonathletes. *Med Sci Sports Exerc.* 2007;39(3):403-409.
59. Paffenbarger RS, Hyde RT, Wing AL, Steinmetz CH. A natural history of athleticism and cardiovascular health. *Jama.* 1984;252(4):491-495.
60. Panayiotoglou A, Grammatikopoulou MG, Maraki MI, et al. Metabolic syndrome in retired soccer players: A pilot study. *Obesity Medicine.* 2017;8:15-22.
61. Park HS, Park JY, Yu R. Relationship of obesity and visceral adiposity with serum concentrations of CRP, TNF-α and IL-6. *Diabetes research and clinical practice.* 2005;69(1):29-35.
62. Perk J, De Backer G, Gohlke H, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). *Eur Heart J.* 2012;33(13):1635-1701.
63. Pokharel Y, Macedo FY, Nambi V, et al. Neck circumference is not associated with subclinical atherosclerosis in retired national football league players. *Clinical Cardiology.* 2014;37(7):402-407.
64. Punjabi NM, Caffo BS, Goodwin JL, et al. Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS medicine.* 2009;6(8):e1000132.
65. Rabkin SW, Leiter L, Reeder BA, Chen Y, Liu L. Risk factor correlates of body mass index. *Canadian Medical Association. Journal.* 1997;157(1):S26.
66. Reiner Ž, Catapano AL, De Backer G, et al. ESC/EAS Guidelines for the management of dyslipidaemias: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). *European heart journal.* 2011;32(14):1769-1818.
67. Ryden L, Standl E, Bartnik M, et al. Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). *Eur Heart J.* 2007;28(1):88-136.
68. Selden MA, Helzberg JH, Waeckerle JF, et al. Cardiometabolic Abnormalities in Current National Football League Players. *American Journal of Cardiology.* 2009;103(7):969-971.
69. Shaw LJ, Raggi P, Schisterman E, Berman DS, Callister TQ. Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality. *Radiology.* 2003;228(3):826-833.
70. Shea JL, Randell EW, Sun G. The prevalence of metabolically healthy obese subjects defined by BMI and dual-energy X-ray absorptiometry. *Obesity (Silver Spring).* 2011;19(3):624-630.
71. Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. *The Journal of clinical investigation.* 2006;116(7):1793-1801.
72. Silva GE, Vana KD, Goodwin JL, Sherrill DL, Quan SF. Identification of patients with sleep disordered breathing: comparing the four-variable screening tool, STOP, STOP-Bang, and Epworth Sleepiness Scales. *J Clin Sleep Med.* 2011;7(5):467-472.
73. Smith SC, Allen J, Blair SN, et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. *Journal of the American College of Cardiology.* 2006;47(10):2130-2139.
74. Somers VK, White DP, Amin R, et al. Sleep apnea and cardiovascular disease: An american heart association/american college of cardiology foundation scientific statement from the american heart association council for high blood pressure research professional education

committee, council on clinical cardiology, stroke council, and council on cardiovascular nursing in collaboration with the national heart, lung, and blood institute national center on sleep disorders research (national institutes of health). *Journal of the American College of Cardiology.* 2008;52(8):686-717.

75. Steffes GD, Megura AE, Adams J, et al. Prevalence of metabolic syndrome risk factors in high school and NCAA division i football players. *Journal of Strength and Conditioning Research.* 2013;27(7):1749-1757.

76. Stein JH, Korcarz CE, Hurst RT, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force endorsed by the Society for Vascular Medicine. *Journal of the American Society of Echocardiography.* 2008;21(2):93-111.

77. Tucker AM, Vogel RA, Lincoln AE, et al. Prevalence of cardiovascular disease risk factors among national football league players. *JAMA - Journal of the American Medical Association.* 2009;301(20):2111-2119.

78. Virani SS, Pompeii L, Lincoln AE, et al. Association between traditional cholesterol parameters, lipoprotein particle concentration, novel biomarkers and carotid plaques in retired National Football League players. *Atherosclerosis.* 2012;222(2):551-556.

79. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg.* 2014;12(12):1495-1499.

80. Warren JM, Ekelund U, Besson H, Mezzani A, Geladas N, Vanhees L. Assessment of physical activity–a review of methodologies with reference to epidemiological research: a report of the exercise physiology section of the European Association of Cardiovascular Prevention and Rehabilitation. *European Journal of Cardiovascular Prevention & Rehabilitation.* 2010;17(2):127-139.

81. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol.* 2018;71(19):e127-e248.

82. Wolf-Maier K, Cooper RS, Banegas JR, et al. Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States. *Jama.* 2003;289(18):2363-2369.

83. Wright CJ, Abbey EL, Brandon BA, Reisman EJ, Kirkpatrick CM. Cardiovascular disease risk profile of NCAA Division III intercollegiate football athletes: a pilot study. *Physician and Sportsmedicine.* 2017;45(3):280-285.

84. Wyman RA, Mays ME, McBride PE, Stein JH. Ultrasound-detected carotid plaque as a predictor of cardiovascular events. *Vasc Med.* 2006;11(2):123-130.

85. Yamamoto JB, Yamamoto BE, Yamamoto PP, Yamamoto LG. Epidemiology of college athlete sizes, 1950s to current. *Research in Sports Medicine.* 2008;16(2):111-127.

86. Yudkin JS, Kumari M, Humphries SE, Mohamed-Ali V. Inflammation, obesity, stress and coronary heart disease: is interleukin-6 the link? *Atherosclerosis.* 2000;148(2):209-214.

87. Zalesin KC, Franklin BA, Miller WM, Peterson ED, McCullough PA. Impact of obesity on cardiovascular disease. Medical Clinics. *Medical Clinics.* 2011;95(5):919-937.

Appendix 1: Study Details

Lead Author (Year)	Study Design	Primary Aims	Setting	Participants	Variables	Risk Factor Prevalence
Miller[50] (2008)	Cross-sectional prevalence	Assess the prevalence of CMS in athletes. Assess the prevalence of CMS based on playing position.	Living heart foundation-health screening, 2004-2006	NFL, n=510 Males Mean Age: 53.8 Sex matched controls from NHANES study LM v NLM	BMI, BF%, SBP, DBP, HT, TC, TG, HDL, LDL, IFG, CMS, Smoking, DM	CMS more prevalent in LM than NLM (59.8% v 30.1%, p=0.001). Elevated BMI, IFG and reduced HDL was more prevalent in LM than NLM.
Panayiotoglou[60] (2017)	Cross-sectional case-control	To determine the risk and prevalence of CMS in retired professional soccer players.	Greece	Soccer, n=12 Males Mean Age: 46.7 Age-sex-BMI matched nonathletic controls	BMI, BF%, WHR, BP snoring, smoking, TG, TC/HDL, nonHDL/HDL	Prevalence of CMS was indifferent between groups. Retired players with CMS gained significantly more weight since retirement.
Barsa[5] (2014)	Cross-sectional	Evaluate the presence and severity of subclinical atherosclerosis. Evaluate whether linemen position is independently associated with an increased risk of subclinical atherosclerosis.	Living heart foundation-health screening, 2007-2009	NFL, n=931 Males Mean Age: 54 No comparators LM v NLM	BMI, WC, SBP, hsCRP, TC, HDL-C, LDL-C, TG, FG, CMS, HT, DM, Smoking, CAC	LM less likely to have absence of CAC (33.8% v 41.7%, p=0.02) and greater likelihood of moderate to severe CAC (32.9% v 26.4%, p=0.04).
Chang[10] (2009)	Cross-sectional	Assess the prevalence of CAC in retired NFL players compared to physically active preventive medicine controls.	Living heart foundation-health screening, 2007	NFL, n=201 Males Mean Age: 51.2	BMI, WC, WHR, SBP, DBP, Fasting insulin, FG, TC, HDL,	No significant difference in the prevalence of CAC (46% v 48.3%, p=0.69) or distribution (p=0.11)

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		Evaluate retired players true risk of an adverse CV event.		Age - sex- BMI-ethnicity matched participants from the DHS and ACLS	LDL, TG, HbA1C, CMS, DM, Smoking, CAC, HT	between retired players and controls.
Hurst[34] (2010)	Cross-sectional	Evaluate subclinical atherosclerosis in retired NFL players. Assess CV risk in professional football players.	Living heart foundation-health screening, 2006-2007	NFL, n=201 Males Mean Age: 50.8 Age-sex- BMI-smoking prevalence matched controls from Mayo clinic, 2006-2007 LM v NLM	BMI, Smoking, HT, SBP, DBP, HL, TC, HDL, LDL, TG, TC/HDL, Glucose, CAP.	Prevalence of CAP in players not significantly different to BMI matched controls (33.3% v 29.3%, p=0.45). CMS more prevalent in LM than NLM (45.8% v 22.5%, p=0.001).
Hyman[35] (2012)	Observational	Validate the accuracy of BMI when measuring obesity in retired NFL population. Investigate the correlation between obesity and several co-morbidities in this population.	An internal medicine practice, May 2010- June 2011	NFL, n=129 Males Mean Age: 42.2 No comparators LM v NLM	BMI, HT, OSA, LVH, DM.	BMI has poor specificity (0.36) in classifying obesity in retired football players. BMI-obesity was correlated to LM (p<0.0001) and OSA (p= 0.0005).
Albuquerque[1] (2010)	Cross-sectional	Assess the prevalence of SDB and HT. Compare the risk of CVD between retired NFL players and controls.	Living heart foundation-health screening, 2006	NFL, n=257 Males Mean Age: 53.9 Age-sex-BMI-matched cohort from the NHANES study	BMI, SBP, DBP, HT, Obesity, TC, TG, HDL, LDL, FG, DM, Smoking, Apnoea - hypopnoea, SDB.	SDB was present in 52.3% of retired players. The prevalence of HT and obesity (p<0.001) were higher in retired players. LM were more likely to have SDB (61.3% Vs 46.6%, p=0.02) and obesity (83.5% Vs 52.5%, p<0.001) compared with NLM. Retired players had lower TC, TG, HDL and IFG than controls.

Carruthers[8] (2017)	Cross-sectional	Assess the 10-y risk of atherosclerotic CVD in elite former athletes.	Not specified	NFL, n=104 Males Mean Age: 53.8 Age - sex matched participants from the DHS	BMI, SBP, Non-HDL, HDL, Median CAC, median ASCVD risk, Smoking.	No significant differences in the odds of having CAC=0 among high ASCVD risk participants (OR 1.37; 95% CI: 0.36, 5.17) nor in the odds of having high CAC (CAC>100) among low ASCVD risk participants (OR 1.28; 95% CI: 0.64, 2.54).
Kelly[38] (2014)	Prospective	Determine the rate of metabolic dysfunction in retired NFL players.	St. John's Health Center, Santa Monica. LA Biomedical Research Institute at Harbour-UCLA medical center.	NFL, n=74 Males Mean Age: 47.3 No comparators Non-hormone deficient v Hormone deficient	BMI, CMS, IGF-1	CMS was present in 50% of retired players. BMI increased significantly (p<0.001) for players during retirement.
Lynch[45] (2007)	Cross-sectional	Determine if playing professional football as a young adult is associated with a more favourable CV risk profile, and a greater bone density and lean body mass compared with their healthy peers.	University of Maryland	NFL, n=16 Males Mean Age: 66 Sex -BMI-race and current physical activity matched never-athletic comparators.	BMI, WC, WHR, BF%, TC, LDL, HDL, TG, Fasting Insulin, Fasting Glucose, BP	Retired players had more favourable body composition and CV risk profile; 37% higher HDL, fourfold higher HDL2, 25% lower TC/HDL ratio, and 31% lower TG than controls (p<0.05 to <0.001).
Pokharel[63] (2014)	Cross-sectional	Examine the association of NC with other markers of adiposity and components of MS. Examine whether NC was independently associated with subclinical atherosclerosis as assessed by CAC and CAP.	Player Care Foundation and the Living Heart Foundation and Boon Heart Institute	NFL, n=845 Males Mean Age: 54 No comparators	HT, DM, SBP. DBP, BMI, NC, WC, FBG, hsCRP, TC, LDL, HDL, TG, CMS, CAC/CAP	21% had CMS, 62% had CAC and 56% CAP present. NC was not associated with CAC or CAP after adjusting for age, race and cardio-metabolic risk factors.

Virani[78] (2012)	Cross-sectional	Assess whether LDL-P concentration and hsCRP can identify subclinical atherosclerosis better than traditional cholesterol parameters. Assess if hsCRP is associated with CAP in retired NFL players. .	Living Heart Foundation and the Boone Heart Institute, September 2007-November 2009	NFL, n=948 Males Mean Age: 53.5 No comparators CMS v No CMS	HT, DM, MS, WC, TC, LDL, nonHDL, TG, LDL-P, HDL, hsCRP	CAP common in retired players (41%) and strongly associated with LDL-P (OR, 3.71, 95%CI: 1.16-11.84). 19.7% of retired players had CMS. Hs-CRP was not associated with carotid plaques (OR: 1.13, 95%CI 0.71-1.79).
Luyster[44] (2017)	Cross-sectional	Compare SA risk in early-middle-aged retired NFL players to a community cohort. Compare risk of SA based on playing position.	Player Care Foundation Cardiovascular Health Screening Program, 2007-2012	NFL, n=122 Males Mean age: 45.3 Age-sex-race-BMI cohort from the CARDIA sleep study	Smoking, WC, BMI, Obese, SBP, DBP, TC, HDL, LDL, TG, DM, FG, Sleep duration, SA risk, CAC	Retired players have a greater prevalence of high SA risk (27% v 11.5%, p=0.002) but similar prevalence of CAC as matched controls (30% v 30%, p=1).

Abbreviations: *ASCVD - atherosclerotic cardiovascular disease; BF%- body fat percentage; BMI- body mass index; ; CAC- carotid artery calcium; CAP- carotid artery plaque; CMS- cardio-metabolic syndrome; DBP- diastolic blood pressure; DM - diabetes mellitus; HDL- high-density lipoprotein; hsCRP- high sensitive C reactive protein; HL-hyperlipidemia; HT- hypertension; IFG- impaired fasting glucose; LM - linemen; LDL- low- density lipoprotein; LDL-P- low-density lipoprotein particle number; NFL- National Football League; NLM - non-linemen; OSA – Obstructive Sleep Apnea; SA – sleep apnoea; SBP- systolic blood pressure; TC- total cholesterol; TG-triglycerides; WC- waist circumference; WHR- waist-hip-ratio.*